

REMARKS

Applicants respectfully request entry of the Amendment and reconsideration of the claims.

Applicants note that a preliminary amendment was filed on February 5, 2004, where claims 8-22 and 24-32 were cancelled, and new claims 33-44 were added. Entry of this preliminary amendment is confirmed in PAIR. Applicants respectfully request the Examiner's acknowledgement and entry of this preliminary amendment.

In the instant response and amendment, Applicants request cancellation of claims 2-3 without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Applicants have amended claims 1, 4-7, 23, and 33-36. Support for the amendments can be found throughout the specification, including at page 10, line 8 to page 11, line 17 and Tables 5 and 7. Applicants have also amended claim 33 to correct an obvious typographical error and 34-36 to ensure proper antecedent basis.

New claims 45-48 have been added. Support can be found throughout the specification including at page 10, lines 20-27 and Tables 5 and 7.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 1-7, 21 and 23 under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Applicants respectfully traverse these rejections.

1. The Examiner rejects claim 2 as indefinite. While not acquiescing to the rejection and solely to expedite prosecution, claim 2 is cancelled, rendering the rejection moot.

2. The Examiner rejects claim 3 for reciting "Table 1, 5, or 7." While not acquiescing to the rejection and solely to expedite prosecution, claim 3 is cancelled, rendering the rejection moot.

3. The Examiner rejects claim 21 for alleged indefiniteness. Applicants respectfully assert that this rejection is moot since claim 21 was cancelled in the preliminary amendment filed on February 5, 2004.

4. The Examiner rejects claims 1-2, 4-7, 21, and 23 for the recitation of "BOG polypeptide." While not acquiescing to the rejection and solely to expedite prosecution, claim 2

and claim 21 are cancelled, rendering the rejection of these claims moot. Applicants have amended "BOG" to recite the full name followed by the acronym in parentheses, "B5T Over-expressed Gene (BOG)." Applicants respectfully request removal of this rejection.

Rejection under 35 U.S.C. § 112, first paragraph (Written Description)

The Examiner rejects claims 1-2, 4-7, 21, and 23 under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description. Specifically, the Examiner alleges that the specification does not provide a correlation between structure and function of the claimed genus of polypeptides (Office Action at p. 5). While not acquiescing to the rejection and solely to expedite prosecution, claim 2 and claim 21 are cancelled, rendering the rejection of these claims moot. Applicants respectfully traverse with respect to claims 1, 4-7, and 23.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, that he or she was in possession of the invention. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ...of the claimed subject matter sufficient to distinguish it from other materials. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. *Id.* at 1406 (emphasis added). Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) *Fed. Reg.* 1099, 1105 (2001); see also, *In re Wertheim*, 191 USPQ 90, 97 (CCPA 1976). The guidelines further state that "[The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an Applicants' disclosure a description of the invention defined by the claims." 66(4) *Fed. Reg.* at 1107; 191 USPQ at 97, (emphasis added). Moreover, in order to have possession of members of a claimed genus, the specification need not describe all of the species that the genus encompasses. *Amgen Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).

Applicants' claim 1 now refers to a BOG polypeptide comprising a sequence at least 90% identical to SEQ ID NO:8, comprising a pRB binding motif, and comprising at least one casein kinase II phosphorylation motif. These structural features are identified in SEQ ID NO: 8. Three species of the claimed genus, namely human, murine, and rat BOG, contain a pRB binding domain comprising the amino acid sequence LXCXE and a casein kinase II phosphorylation site comprising the amino acid sequence STDD (Specification at Table 8). BOG polypeptides containing these structural features compete with and displace E2F bound to pRB. (Specification at Example 3, page 45, lines 15- 16 and Fig. 2C). Displacement of E2F from pRB leads to transcriptional activation of growth promoting genes resulting in unrestricted cell growth (i.e. cancer). Applicants respectfully assert that these teachings demonstrate possession of the genus of the claimed BOG polypeptides. The amino acid homology, the conserved pRB binding domain, and the conserved casein kinase II phosphorylation site are structural features that are common to the members of the genus of BOG polypeptides and are correlated to a function of the polypeptide.

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of the pending rejections under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description.

Rejection under 35 U.S.C. § 112, first paragraph (Enablement)

The Examiner rejects claims 1-2, 4-7, 21 and 23 under 35 U.S.C. § 112, first paragraph, for an alleged lack of enablement. While not acquiescing to the rejection and solely to expedite prosecution, claims 2 and 21 are cancelled, rendering the rejection of these claims moot. Applicants respectfully traverse this rejection with respect to claims 1, 4-7, and 23.

To meet the enablement requirement of 35 U.S.C. § 112, first paragraph, a specification must contain a sufficient description to enable one skilled in the art to make and use the claimed invention (*See, e.g., Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1253 (Fed. Cir. 2004); MPEP §2164.01). A specification does not need to explicitly disclose every detail, and may omit what is well known in the art (*In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991); MPEP 2164.01). To make and use an invention may require experimentation even if the specification is enabling (*In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *Atlas Powder Co. v. E.I. du Pont*

de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984); MPEP §2164.01). The experimentation must not be unduly extensive (*Id.*), however, costly and timely experimentation alone does not constitute undue experimentation. (*U.S. v. Teletronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988)).

Applicants respectfully contend that the specification teaches how to make and use BOG polypeptides without undue experimentation. Applicants have amended claim 1 to refer to a BOG polypeptide comprising a sequence at least about 90% identical to SEQ ID NO:8, a pRB binding motif, and a casein kinase II phosphorylation motif. Applicants have provided polypeptide sequences as well as structural features of the BOG polypeptides such as the pRB binding motif and casein kinase II phosphorylation motif (Tables 1-3, 5, and 7-8). Applicants also submit they have provided working examples using the claimed polypeptides. Examples 2 and 3 demonstrate BOG interactions with pRB and its effects (e.g., displacing E2F-1). Example 4 demonstrates the effects of BOG expression. For example, Applicants have described that overexpression of BOG completely blocks the growth inhibitory effects of TGF- β 1, which exerts its cell cycle control via pRB. A hallmark of cancerous liver cells is an increased expression of BOG. Applicants also demonstrate a BOG fusion protein in Example 6 and then use said BOG fusion protein to produce antibodies specific for BOG binding in Example 7. These antibodies are at least useful to detect overexpression of BOG in cancer and other types of cells. In Example 9, Applicants demonstrate the detection of BOG expression during cell cycling. For at least these reasons, Applicants respectfully assert that the specification enables the claims without undue experimentation.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for an alleged lack of enablement.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejects claims 1-4 and 21 under 35 U.S.C. § 102(b) as allegedly being anticipated by Phillips *et al.* (*J. Gen. Virol.*, 78:905-909 (1997)). "Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim." *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *See also*, MPEP §2131. Claims 2-3 and 21

have been cancelled rendering the rejection of these claims moot. Applicants respectfully traverse this rejection with respect to claims 1 and 4.

Applicants have amended claim 1 to refer to a BOG polypeptide comprising at least about 90% amino acid sequence identity with SEQ ID NO: 8. The Examiner cites a sequence of serine-serine in the E7 protein. The HPV-16 E7 protein sequence is GenBank Accession No. AAO85409. This 98 amino acid E7 sequence only has 16 identical residues to SEQ ID NO:8 when aligning the two polypeptide sequences using ClustalW 1.8. Hence, Phillips et al. do not disclose each and every claim limitation. For at least this reason, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 6-7 and 23 under 35 U.S.C. § 103(a) as allegedly being obvious over Phillips *et al.* (*J. Gen. Virol.*, 78:905-909 (1997)), in view of U.S. Patent No. 5,188,943 (Reddington et al.). To establish a *prima facie* case of obviousness, the prior art reference(s) must teach or suggest all the claim limitations. MPEP §2143; *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Applicants respectfully traverse this rejection.

Applicants respectfully assert that the cited prior art does not teach or suggest all of the claim limitations. In this rejection, the Examiner applies the same teachings of Phillips et al. as recited in her rejection under 35 U.S.C. § 102(b). As discussed above, Phillips et al. teaches the HPV-16 E7 protein, which does not share 90% sequence identity to SEQ ID NO:8. The HPV-16 E7 protein sequence is GenBank Accession No. AAO85409. This 98 amino acid E7 sequence only has 16 identical residues to SEQ ID NO:8 when aligning the two polypeptide sequences using ClustalW 1.8. Moreover, the protein is a viral protein and does not teach or suggest that a non-viral protein has similar structure or function. For at least this reason, Applicants respectfully assert that the Examiner has not established that the prior art teaches or suggests all of the claim limitations, and thereby has not established a *prima facie* case of obviousness. Hence, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(1).

Summary

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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